Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION AND STEP THERAPY POLICY AND CRITERIA ORPTCCNS065.0824	**CENTRAL NERVOUS SYSTEM DRUGS** **MEDICALLY ADMINISTERED MULTIPLE SCLEROSIS AGENTS** See Table 1 for Applicable Medications
Effective Date: 10/1/2024	**Review/Revised Date**: 07/24 (JN)
Original Effective Date: 11/23	**P&T Committee Meeting Date**: 08/23, 08/24
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Medicare Part B

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications

REQUIRED MEDICAL INFORMATION:
For initiation of therapy for **multiple sclerosis (MS)**, all the following criteria (1-2) must be met:

1. Must have one of the following confirmed diagnoses:
    a. Relapsing-remitting multiple sclerosis (RRMS)
    b. Secondary progressive multiple sclerosis (SPMS)
    c. Clinically isolated syndrome (CIS)
    d. For Ocrevus only: Primary progressive MS
2. Documentation of ONE of the following (a b, c, or d) for RRMS, SPMS, CIS:
    a. Documentation the patient has highly active disease defined as ONE of the following:
        i. Greater than or equal to two relapses in the previous year
        ii. The patient has greater than or equal to one gadolinium enhancing lesion on MRI
        iii. Presence of significant T2 lesion burden defined as ONE of the following:
            1) Greater than ten (10) T2 lesion burden as documented with MRI
            2) Significant increase in T2 lesion load compared with a previous MRI
            3) T2 lesion(s) located in spinal cord or brainstem

b. The patient has been treated with at least three multiple sclerosis agents from different drug classes
c. Inadequate response (after at least six months of continuous therapy) or intolerance to one of the following: generic dimethyl fumarate, generic glatiramer/Glatopa®, generic fingolimod, or generic teriflunomide
d. FDA labeled contraindication to ALL of the following: generic dimethyl fumarate, generic glatiramer/Glatopa®, generic fingolimod, and generic teriflunomide

For **patients established on therapy** (within the previous year), the following must be met: Documentation of positive clinical response to therapy

EXCLUSION CRITERIA:
Concurrent use with other disease modifying agents for multiple sclerosis

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS:
Must be prescribed by or in consultation with a neurologist.

COVERAGE DURATION:
Initial authorization will be approved for one year. Reauthorization will be approved until no longer eligible with the plan, subject to formulary and/or benefit changes

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Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case

INTRODUCTION:

Ublituximab-xiiy (Briumvi®), a B-cell therapy with CD20-directed cytolytic monoclonal antibody for treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Ublituximab-xiiy is administered every 24 weeks (6 months).

Ocrelizumab (Ocrevus®), a B-cell therapy with CD20-directed cytolytic monoclonal antibody for treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults, and primary progressive MS in adults.

FDA APPROVED INDICATIONS:
Ublituximab (Briumvi®) is indicated for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Ocrelizumab (Ocrevus®) is indicated for the treatment of relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults, and primary progressive MS in adults.

Table 1. Medically infused multiple sclerosis medications

Drug	Class	RRMS	SPMS	CIS	Other
ublituximab (Briumvi®)	Recombinant monoclonal antibody, binds to CD52, natural killer cells, monocytes, and macrophages	X	X	X	
Ocrelizumab (Ocrevus®)	Immune modulator, binds to CD-20	X	X	X	Primary progressive MS

MOA = mechanism of action, RRMS = relapsing-remitting multiple sclerosis, SPMS = secondary progressive multiple sclerosis, CIS = clinically isolated syndrome

POSITION STATEMENT:
Guidelines for Multiple Sclerosis include the American Academy of Neurology Publication “Comprehensive Systematic Review Summary: Disease-Modifying Therapies for Adults with Multiple Sclerosis” published in 2018 and a consensus paper by the Multiple Sclerosis Coalition titled “The Use of Disease-Modifying Therapies in Multiple Sclerosis” published in 2019. Guidelines state that initiating a disease modifying therapy (DMT) should be offered to patients as early as possible. The choice of initial DMT should be individualized to consider safety, route of

administration, lifestyle, cost, efficacy, adverse effects (AEs), and tolerability. When switching therapies after failure of an agent, disease activity, adherence, AE profiles, and mechanisms of action should be considered when selecting a new agent to start. For advanced, aggressive, or highly active disease guidelines recommend fingolimod (Gilenya®), natalizumab (Tysabri®), ocrelizumab (Ocrevus®), or alemtuzumab (Lemtrada®). Additionally, guidelines state categorize DMT therapies for evidence for lowering relapse rate (see Table 2).[5]

Table 2. DMT Evidence for Lowering Relapse Rate[5]

Very Low	Low	Moderate	Strong
Immunoglobulins	Cyclophosphamide	Azathioprine	Alemtuzumab
Methotrexate	Mycophenolate Mofetil	Interferon beta-1b	Cladribine
Rituximab			Dimethyl Fumarate†
Corticosteroids			Fingolimod†
			Glatiramer Acetate†
			Interferon beta-1a
			Mitoxantrone
			Natalizumab
			Ocrelizumab
			Pegylated Interferon
			Teriflunomide†

† Generic Available

REFERENCE/RESOURCES:

1. Briumvi package insert. Morrisville, NC: TG Therapeutics, Inc; 2023 Jan.
2. Ocrevus package insert. San Francisco, CA: Genentech, Inc; 2024 July.
3. Briumvi. In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically.
4. Ocrevus. In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically.
5. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis. Neurology 2018;90:777–788.